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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,966	03/22/2002	Reiner Grabowski	216180	4911
23460	7590	11/14/2005		
LEYDIG VOIT & MAYER, LTD TWO PRUDENTIAL PLAZA, SUITE 4900 180 NORTH STETSON AVENUE CHICAGO, IL 60601-6780			EXAMINER CALAMITA, HEATHER	
			ART UNIT	PAPER NUMBER
			1637	

DATE MAILED: 11/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/088,966	Applicant(s) GRABOWSKI ET AL.	
	Examiner Heather G. Calamita, Ph.D.	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 September 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 86-106 is/are pending in the application.
- 4a) Of the above claim(s) 90, 95, 99, 101, 104 and 106 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 86-89, 91-94, 96-98, 100, 102, 103 and 105 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>March 22, 2002</u> | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. Claims 86-106 are currently pending. Newly submitted claims 90, 95, 99, 101, 104 and 106 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: These claims are drawn to methods with SEQ ID NOs 1 or 211 and 212. The originally claimed invention was drawn to methods with SEQ ID NOs 2 and 25.

Since applicants have received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 90, 95, 99, 101, 104 and 106 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 86-89, 91-94, 96-98, 100, 102, 103 and 105 are currently under examination. These claims are directed to methods which continue to recite limitations not directed to the elected subject matter of SEQ ID NOs 2 and 25. These claims are under examination only as they are directed to methods with the previously elected subject matter of SEQ ID NOs 2 and 25. This application contains subject matter drawn to an invention nonelected with traverse in the response filed on March 24, 2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Finally, any objections and rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 86-89, 91-94, 96-98, 100, 102, 103 and 105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mariani et al. (USPN 5,654,141, 08/05/1997) in view of Yamamoto et al. (Genebank Accession number AB001341, submitted January 25, 1997).

With regard to claim 86, Mariani et al. teach a method for detecting bacteria in an analytical sample, comprising

the step of bringing the analytical sample into contact with an added nucleic acid or a combination of added nucleic acids, and detecting suitable hybrid nucleic acids comprising the added nucleic acid and bacterial nucleic acid wherein the one or more added nucleic acid is SEQ ID NOs 2 and or 25. (see col. 2 lines 10-16).

With regard to claims 87 and 91, Mariani et al. teach the bacteria are enterobacteria (see col. 2 lines 52 and 54 and example 1). *E. coli* are enterobacteria.

With regard to claims 88 and 93, Mariani et al. teach the process involves a PCR amplification of the nucleic acid to be detected (see col. 5 lines 40-44).

With regard to claims 89 and 94, Mariani et al. teach in that the process involves a Southern Blot hybridization (see col. 8 lines 8-9).

With regard to claim 92, Mariani et al. teach a method for amplifying bacterial DNA of a multiplicity of different taxonomic units, especially genera and species, using primers in which in a first amplification step the DNA for high taxonomic units such as classes, phyla or families is amplified with conserved primers (see col. 4 lines 21-29, and 38-43). The 16S rRNA gene is conserved, and the target nucleic acids are from the classes of *Escherichia*, *Streptococcus*, *Staphylococcus* and *Bacteroides*. And, optionally, in a further step, the DNA fragments obtained by amplification which are specific for genera or species are detected by means of probes, wherein the primers used comprise SEQ ID NOs 2 and 25 (see col. 8 lines 39-56).

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With regard to claim 97, Mariani et al. teach the one or more added nucleic acid molecule or molecules is modified or labeled so that it can generate a signal in analytical detection procedures, with the modification being fluorescent (see col. 8 lines 1-20).

With regard to claims 86-89, 91-94, 96-98, 100, 102, 103 and 105, Mariani et al. do not teach SEQ ID NOs 2 and 25 as the primer pair.

Yamamoto et al. teach SEQ ID NOs 2 and 25 (see alignment below).

Claimed SEQ ID NO: 2 1 ttcgggttgatcatgccaatg 20

Yamamoto et al. 11799 ttcgggttgatcatgccaatg 11780

Claimed SEQ ID NO: 25 1 ccgccaggcaaattctgt 18

Yamamoto et al. 11482 ccgccaggcaaattctgt 11499

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the method of Mariani with the use of functionally equivalent primers selected from the sequences of Yamamoto since Mariani expressly teaches primer selection using primers which amplify specific sequences in *E. coli* in order to detect the presence of the bacteria in patient samples.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers for the detection of *E. coli* and concerning

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which a microbiologist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Response to Arguments

3. Applicant's arguments filed September 16, 2005, have been fully considered but they are not persuasive.

Applicants argue the 103 (a) rejection of the claims is improper because the rationale amounts to an invitation to experiment or an obvious to try situation and possibly involves hindsight reasoning. This is not persuasive because Buck shows every 18 mer primer selected over 300 base pairs was successful. This leads to the expectation of success for amplification or extensions. In the recent court decision *In Re*

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Deuel 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious.

Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers for the detection of *E. coli* and concerning which a microbiologist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations and the 103 (a) rejections are proper and therefore maintained.

Conclusion

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Correspondence

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

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JEFFREY FREDMAN
PRIMARY EXAMINER
11/8/05